

Whole-body MRI

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INTRODUCTION

Fundamental to the diagnosis of disease is the visualization of the entire body to detect diseases of different organ systems. Whole-body imaging can be pursued in essentially two different subject groups, normal subjects to evaluate for a range of benign and malignant disease processes, and patients with a known malignancy or other disease process to evaluate the extent of disease. The intention of screening in the first group is to detect a wide range of diseases only, before they become clinically manifest. Thus, treatment is much more likely to result in a better outcome regarding morbidity, mortality, and quality of life than if it were diagnosed later. In the second group with known malignancy, possible therapeutic strategies depend on the stage of disease and whether multiple organ systems have been affected. In the past, patients had to undergo a variety of different diagnostic procedures to achieve a whole-body staging or screening, including imaging studies such as ultrasonography, CT, MRI, positron emission tomography (PET) and X-ray examinations. The combination of procedures is often time-consuming and inconvenient for the patient. Thus, a single imaging examination providing information of different organ systems (ideally of the entire body) would be of great interest.

TECHNICAL REQUIREMENTS FOR WHOLE-BODY MRI

Whole-body MRI has been evaluated in research investigations in the past. However, it has not been used in routine clinical care either because of extensively long examination times when diagnostic quality sequences are employed, or because of inferior quality when fast sequences are employed. To achieve adequate diagnostic quality one major time-consuming problem was that patients had to be repositioned in the bore of the magnet, with different surface coils for each anatomical region. To overcome these problems, different strategies have been explored. One approach has been the implementation of a sliding table platform that enables data acquisition of different anatomical regions in rapid succession. Signal reception can be accomplished using posteriorly located spine coils (integrated in the patient table) and an anteriorly positioned torso phased-array coil, which remains fixed to the stationary patient table in the isocenter of the magnet. Hence, data acquisition can be performed with the same stationary coil set. A rolling table platform has been successfully employed for the detection of bone metastases, parenchymal metastases including hepatic, cerebral and lung metastases and whole-body MR-angiography.

Other technological advances provide MRI systems with multiple input channels, which allow the simultaneous use of specialized surface coils. Thus, high-

resolution images can be acquired of multiple regions of the body without the need of coil repositioning. Usually, between 5 and 6 sets of specialized surface coils are used: one head and neck coil, two or three phased array coils (depending on the patient's size) to cover the thorax, abdomen and pelvis and one peripheral MR-angio coil. Automatic table motion can acquire a total scan range of over 200cm in the z-axis. This MR unit has been evaluated in initial feasibility studies for the assessment of metastatic and vascular disease.

Beyond the technical improvements in system hardware, concurrent developments have been made in MRI sequence protocols and imaging techniques. Earlier generation whole-body MRI concepts were based on the acquisition of fast echoplanar imaging (EPI) with limited spatial resolution and diagnostic accuracy. The more recent development of high quality single-shot echo-train spin-echo imaging still allows for very short image acquisition time, but with diagnostically acceptable image quality. Another important innovation is fat suppressed three-dimensional (3D) gradient echo (GRE) sequences with nearly isotropic resolution, which has been developed for parenchymal imaging. These 3D data sets can be acquired as a single breath-hold and provide image quality similar to that of conventional fat-suppressed two-dimensional (2D) GRE images. Furthermore, 3D data also offers the advantage of multiplanar reconstructions. In conjunction with rapid table motion, these T1w sequences permit dynamic imaging of different parenchymal organs after an intravenous injection of paramagnetic contrast agents.

Further improvement of whole-body MR is achieved using parallel acquisition techniques (PAT). These techniques allow data acquisition with either increased spatial resolution or decreased acquisition time, or a combination of both. Combining a high number of surface coil elements and receiver coils now enables PAT imaging in all three spatial directions. Clinical implementation of high PAT factors is expected in the near future. Thus, the combined effect of hardware and sequence advances has allowed whole-body MRI to be performed more rapidly, within a time period of 10-20 minutes, while maintaining diagnostic image quality.

MRI SEQUENCE PROTOCOLS FOR WHOLE-BODY IMAGING

Examination protocols should be tailored to specific clinical circumstances. Healthy subject should undergo a different protocol for screening than patients with malignancy for staging. However, the foundation for all whole-body protocols should represent gadolinium enhanced T1w 3D GRE of all different organ systems. Whole-body MRI using only unenhanced imaging would substantially shorten examination times, but diagnostic accuracy would also diminish. Data collection should be started in the abdomen with an arterial, portal venous and late venous contrast phase of the liver. Further data acquisition may be chosen according to the individual need of the patient. Thus, it might be reasonable to include sequences for the assessment of the gastrointestinal tract in a patient with previous history or known colorectal carcinoma, or to increase coverage of data acquisition in MR Angiographic (MRA) protocols.

Other authors propose additional acquisition of further sequences including STIR for the assessment of the skeletal system and the pelvis, or FLAIR for the evaluation of the brain. STIR can also be obtained as an echo-train sequence to obtain further time savings.

CLINICAL EXPERIENCES OF WHOLE-BODY MRI FOR STAGING PURPOSES

Initial studies describing whole-body MRI focused on the detection of osseous metastases in patients with primary malignancies that had the potential to metastasize to the skeletal system. Radionuclide scintigraphy served as the reference standard in these studies. Dedicated MRI had been found to be more accurate in the detection of bone metastases compared to scintigraphy. In a trial by Eustace et al., MRI revealed superiority for the depiction of bone metastases: sensitivity of MRI and skeletal scintigraphy were 96% and 72%, respectively. Short tau inversion recovery (STIR) sequences were observed to be particularly effective for detecting bone metastases. The use of STIR sequences in conjunction with whole-body MRI has been evaluated in a preliminary trial. The MRI exam was divided into five regions to ensure coverage from the head to the upper half of the tibia and fibula. In all regions STIR sequences were acquired in the coronal plane during quiet respiration. The described protocol was performed within less than 30 minutes. In the detection of skeletal metastases, distinct regional advantages and disadvantages were observed for both skeletal scintigraphy and whole-body-MRI. Scintigraphy proved more sensitive in the assessment of the ribs, scapula and skull. However, scintigraphy has some important limitations including; exposure to ionizing radiation, difficulty in differentiating degenerative disease and healing fractures from metastases. In addition, the relative activity of osteoblasts and osteoclasts affects how well metastases are detected by scintigraphy. Regarding MRI, the detection rate for osseous metastases in the spine and the pelvis was found to be superior to skeletal scintigraphy. Nevertheless, using STIR sequences for whole-body MRI has important drawbacks: the technique is still relatively time consuming, owing to the long acquisition times at each station. Concomitant disease of parenchymal organs including the brain, lung and liver is not adequately studied with this sequence alone. Eventually, the interpretation of STIR images alone is not very specific, because also benign lesions may show high signal intensity.

To justify the expense of whole-body MRI, the range of diagnostic capabilities must be broad. Imaging must be performed to detect not only osseous metastases but also metastases in all other organ systems. This may be achieved by 3D-GRE images with nearly isotropic resolution and gadolinium enhancement. Data acquisition is accomplished in breath hold periods, rendering image quality consistent. An initial study including 8 patients with malignant tumors showed the feasibility of using contrast-enhanced T1w 3D GRE sequences for whole-body imaging. Good correlation with standard staging examinations including CT and bone scintigraphy was observed. Dynamic imaging of the liver was accurate for the detection and characterization of hepatic mass lesions, as previously shown in other studies. The other abdominal organs, including the pancreas, adrenal glands and kidneys were imaged by MRI with a high level of diagnostic accuracy, concurring with findings from prior studies. Cerebral and osseous lesions were also well shown as enhancing focal lesions. In this preliminary study, all cerebral and osseous metastases shown by the reference examinations were correctly depicted. Image quality of the lungs proved to be slightly inferior to CT scanning. All pulmonary metastases except a single small lesion were correctly detected. These results are confirmed by other authors indicating that lesions larger than 5mm in size can be adequately depicted by MRI.

A follow-up study described a larger patient cohort, comprising 51 patients with known malignant tumors. The most common primary tumors were breast cancer, lung cancer and testicular cancer, which all have the propensity to metastasize to different organ systems including brain, lungs, liver, lymph nodes and bones. Reference staging was based on CT, dedicated MRI and nuclear scintigraphy. In addition to gadolinium-enhanced 3D-GRE of the entire body, supplemental imaging of the thorax and abdomen was acquired with fat-suppressed T2-weighted single-shot echo-train spin-

echo. Mean scanner time for whole-body MRI was approximately 15 minutes including the time for patient set up and the acquisition of all data sets. All 43 patients who were proven to have metastatic disease were found to have metastases on whole-body MRI. Interestingly, the reference examinations revealed metastatic disease in only 42 patients. In one patient with a single hepatic metastasis, which was subsequently proven by histology, only whole-body MRI was able to depict this lesion. There were distinct differences in the sensitivity of metastases detection depending on the anatomical region. More liver metastases were shown on MRI than on CT. Whole-body MRI did not reveal some lung lesions detected by CT, however all these pulmonary nodules were smaller than 6 mm. The benefit of detecting small pulmonary nodules is controversial since the great majority is benign. Many patients with these benign lesions undergo serial follow up CT with the attendant risks of repeat radiation exposure. The requirement for serial follow up stems from the fact that CT cannot be used to differentiate between small malignant and benign lung lesions. Compared to using only gadolinium-enhanced 3D-GRE images the addition of T2w sequences may improve the diagnostic information of lung disease. The value of T2 weighted images for MR imaging of the lungs has been documented in other studies. Concerning skeletal imaging for osseous metastases detection, a higher total number of bone metastases were detected on MRI compared to skeletal scintigraphy. Similar to the findings reported on prior studies using whole-body MRI with STIR sequences, there were regional advantages and disadvantages in bone metastases detection. Compared to scintigraphy, MRI showed superior detection of osseous metastases located in the spine and pelvis whereas some metastases in the ribs were missed. A high accuracy for the detection of metastases in other organ systems was observed. All metastases depicted in the cerebrum and in the adrenal glands by reference examinations were detected by whole-body MRI as well. Mediastinal or abdominal lymph node metastases were considered present in 15 patients on whole-body MRI, and all findings were confirmed by CT scans. Only one patient showed a mediastinal lymph node metastasis on CT, which had not been detected by MRI.

In another study whole-body MRI was compared to dual-modality PET/CT in patients with a variety of malignancies. Both modalities showed high accuracy using TNM staging. The extent of primary tumors and lymph nodes metastases was more reliably staged with PET/CT, while whole-body MRI was more sensitive and specific in the detection of hepatic and skeletal lesions. PET/CT performed particularly well in staging patients with primary lung cancer, which was the largest group of cancer histology type in this study, reflecting the utility of this modality in this patient group.

The recent hardware developments of multiple phased-array surface coils and receiver channels combined with parallel imaging will offer further dramatic reduction in data acquisition times thereby permitting acquisition of more different types of sequences while maintaining short study times. Schlemmer et al. described a whole-body protocol that included STIR sequences for the assessment of the skeletal system and the pelvis, FLAIR (fluid attenuation inversion recovery) sequence for the evaluation of the brain and gadolinium-enhanced T1w 3D-GRE with fat suppression for all regions. The study comprised 63 patients with known metastatic disease. By means of MRI revealed more lesions than CT particularly in the brain, liver and bone marrow. Due to the results of whole-body MRI, therapeutic strategies were modified in 10% of the subjects.

In summary, whole-body MRI using T2w and contrast-enhanced T1w imaging includes all properties needed for metastases staging: it is fast, provides high quality MR data and allows reliable detection of metastatic disease in different organ systems.

WHOLE-BODY SCREENING

Screening is defined as the systematic examination to detect unsuspected disease. Subjects without clinical symptoms undergo screening examinations. This should be differentiated from staging procedures in patients with a known disease to assess whether other organ systems are affected by the primary pathology.

Summarizing the experience of MRI studies for staging it appears that MRI is superior to CT for imaging the liver, whereas CT is superior for imaging the lungs. MRI also appears superior to nuclear scintigraphy and to CT for the detection of osseous metastases. Of course, a screening population is different than a population that undergoes staging. High accuracy in a staging population does not necessarily imply high accuracy for screening. However, first experiences underline the potential of whole-body MRI for screening. In the case that an individual harbours some serious disease, it can affect that subject's longevity if the disease was found at an early stage. However, treatment for the screened diseases must be proven to affect the natural course of the disease. Statistically, only a limited number of patients without clinical symptoms will have a serious underlying disease. Therefore, it is mandatory that a screening examination is very sensitive so as not to miss any important findings in all organ systems. Furthermore, it must be very specific in order to limit the number of false-positive results and to reduce the number of additional dedicated follow-up examinations.

Another important question is when to perform a screening study and what to look for. Whole-body screening usually cannot be as accurate as a dedicated diagnostic MRI examination, which may look at a specific organ in great detail. At present, detailed imaging of the entire body and of all organ systems would be prohibitively long, even on the newest MR machines. The solution at present should be based on a compromise: either to concentrate on organ systems tailored to the risk profile of a patient, or to look for the most common lethal diseases in general (e.g. colon, lung and breast cancer). Additionally, whole-body MRI should be considered a part of an entire picture of diagnostic screening tests. This would also include blood tests (such as prostate specific antigen level), and other laboratory tests.

Goehde et al have proposed a whole-body MRI concept encompassing the assessment of the brain, the arterial system, the heart and the abdomen incorporated into one study. A total of 298 subjects without a history of serious illnesses were studied with a mean examination time of approximately one hour. Several important findings with therapeutic consequences were identified including vascular diseases and malignancies. However, this protocol did not include MR sequences to detect important diseases such as breast or prostate cancer. Expanding the screening to rarer diseases or very small lesions (e.g. pituitary tumors) would make the entire procedure cumbersome, if not impractical due to time constraints.

In addition to screening for malignant disease in healthy subjects, there are other rationales for using whole-body MR imaging. MR angiography has been shown to provide high diagnostic accuracy for the assessment of most vascular territories. Whole-body MR angiography is an intriguing concept as atherosclerotic disease may affect many different arterial vessels at the same time, in addition to the symptomatic territories. Whole-body MRI has been evaluated for the detection of clinically important atherosclerotic lesions. Goyen et al. examined 100 patients with known peripheral vascular disease using a whole-body protocol. Five slightly overlapping 3D data sets were acquired with a bolus chase technique following the intravenous administration of gadolinium. In addition to the known peripheral vascular disease, additional arterial lesions were found in 25% of the patients, including renal arteries, carotid arteries, and subclavian arteries. The clinical importance of mild arterial stenoses is open to question. Furthermore, there are still limitations of MRI regarding the display of

coronary arteries. Although various authors claim this technique to have tremendous potential, it has not yet achieved clinical appreciation. However, MR angiography should be part of a more comprehensive screen for disease.

LIMITATIONS OF WHOLE-BODY MRI

In addition to the compelling aspects of whole-body MRI, especially the high soft tissue contrast resolution and the lack of ionizing radiation, there are limits and drawbacks. MRI provides only fair accuracy in the assessment of certain organs, including the lungs and prostate. MR imaging of these structures may be currently limited, but there is ongoing development into new MR techniques, for example MR spectroscopy for the depiction of prostate cancer.

Another problem is the detection of lesions that are indeterminate, and the requirement of follow-up examinations or, in selected cases, a surgical procedure. This may be especially problematic with small pulmonary nodules. The time course necessary for follow up of many indeterminate lesions is still undergoing evaluation, and follow up studies add more cost to an already expensive diagnostic procedure.

Who will interpret whole-body MRI is also to be determined. Interpretation is complex and time-consuming. Will it be a single radiologist trained in all subspecialty organ systems, or optimally, different radiologists with different subspecialty training? Whole-body MRI is also best performed on current generation MR systems, whose availability is still limited. MRI is intrinsically relatively expensive because of the different components of the system and the requirement for liquid helium and nitrogen. There is still no reliable data on the real cost / benefit ratio of whole-body MRI. However, more high-performance scanners will be installed, and the costs associated with maintaining MRI systems and thereby the costs for each examination will substantially decrease in the coming years.

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